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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,872	09/29/2005	Tatsuo Hoshino	21407 US C038435/0185010	2413
7590 Stephen M Haracz Bryan Cave 1290 Avenue of the Americas New York, NY 10104			EXAMINER MEAH, MOHAMMAD Y	
			ART UNIT 1652	PAPER NUMBER
			MAIL DATE 07/31/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/528,872	Applicant(s) HOSHINO ET AL.	
	Examiner Mohammad Meah	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 27-32 is/are pending in the application.
- 4a) Of the above claim(s) 1-11 and 32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 27, 30-31, 33-40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-11 were examined in the previous action. With supplemental amendment of this application, the applicant, on dates 4/17/07, cancelled claims 12-26, amended claims 1-4, 8-11 and added new claims 27-40. However claims 1-11 have been amended to be within non-elected group VII of the restriction requirement sent 7/31/06 and new claim 32 is within the scope of Group VI and therefore claims 1-11 and 32 are withdrawn as non-elected. New claims 27-31 and 33-40 are within elected group and therefore will be examined here.

Priority

Acknowledgement is made of applicant's priority date based on application filing date of 09/23/2003 for PCT/EPO3/10573 and foreign application EPO 02021619.8, filed 09/27/02.

Claim Rejections

35 U.S.C. 112 1st paragraph written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27, 30 and 33-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules having 90% sequence identity with SEQ ID NO: 2. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

35 U.S.C. 112 1st paragraph enablement rejections

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27, 30-31, 33-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the DNA of SEQ ID NO: 2 or a DNA encoding polypeptide of SEQ ID NO: 3 or a DNA encoding a protein having 95% sequence identity with SEQ ID NO:3 having squalene synthase activity, does not reasonably provide enablement for any DNA molecules having 95% SEQ ID NO: 2 or any DNA which will hybridize to SEQ ID NO: 2 under the said stringent condition described in the claims and which has squalene synthase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, use the invention commensurate in scope with these claims.

Claims 27, 30-31, 33-40 are so broad as to encompass any DNA molecules having 95% SEQ ID NO: 2 or any DNA which will hybridize to SEQ ID NO: 2 under the said stringent condition described in the claims and which has squalene synthase activity and host cells transformed with said DNAs and methods of producing the encoded protein of said DNAs. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number DNAs that encode amino acids sequences of proteins broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

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However, in this case the disclosure is limited to the nucleotide sequence that encodes the amino acid sequence of only one squalene synthase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any nucleic acid that encode amino acids sequences of proteins broadly encompassed by the claims because the specification does not establish: (A) regions of the protein structure which may be modified without effecting squalene synthase activity; (B) the general tolerance of squalene synthase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any squalene synthase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated

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with the scope of the claims broadly including DNA that encode an enormous number of amino acid modifications of the enzyme of SEQ ID NO: 3. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of squalene synthase genes, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants arguments against rejection of the claims under 35 USC 112 first paragraph enablement requirement are acknowledged but not found persuasive as explained above. Although the specification is enabling for the DNA of SEQ ID NO: 2 or a DNA encoding polypeptide of SEQ ID NO: 3 or a DNA encoding a protein having 95% sequence identity with SEQ ID NO:3 or DNA which will hybridize to SEQ ID NO: 2 under high stringent condition (washing at least at 65 °C) having squalene synthase activity, does not reasonably provide enablement for any DNA molecules having 95% SEQ ID NO: 2 or any DNA which will hybridize to SEQ ID NO: 2 under high stringent condition (washing at least at 65 °C) described in the claims. Because as explained in prior rejection and also above the genus of DNAs claimed in the instant claims are broad variants of DNAs that specification do not describe. To find out which DNA among these enormous number of DNAs that encode a squalene synthase would be required the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation. While enablement is not

precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification

CLAIM Rejection - 35 U.S.C 102

Rejection of claims 27-31 and 33-40 as being anticipated under 35 U.S.C. 102(b) by Robinson et al. (Mol & cell boil 1993, pp 2706-2717). Is withdrawn after applicants' amendments and arguments.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah, PhD

Examiner, Art Unit 1652

Recombinant Enzymes, 3C31 Remsen Bld

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Application/Control Number: 10/528,872

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A handwritten signature in black ink, appearing to read 'Achutamurthy', with a long horizontal flourish extending to the right.

PONNATHAPUACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600